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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/575,217	05/07/2007	Christof Niehrs	025953-001	6923

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EXAMINER	
MARVICH, MARIA	

ART UNIT	PAPER NUMBER
1633	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/575,217	NIEHRS ET AL.	
	Examiner	Art Unit	
	MARIA B. MARVICH	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 September 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *9-28,30 and 31* is/are pending in the application.

4a) Of the above claim(s) *9 and 11-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10,21-28,30 and 31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 October 2007* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This office action is in response to an amendment filed 9/7/10. Claims 9-28, 30 and 31 are pending.

This application contains claims 9 and 11-20 drawn to an invention nonelected with traverse in the reply filed on 12/18/09. Therefore, claims 10, 21-28, 30 and 31 are under examination.

The amendment to include SEQ ID NO:s to claims 3, 4 and 6 as well as to pages of the specification are sufficient to place the application in sequence compliance. As well, the amendments to replace figures 15 and 16 are sufficient to overcome the objections to the drawings.

Claim Objections

Claims 10, 21 and 30 are objected to because of the following informalities: for completeness, claim 10 should be amended to recite --wherein if the compound binds to SEQ ID NO:26, the compound is a binding partner of SEQ ID NO:26--.

In claim 21, the method is directed to identifying a binding partner that affects the activity of Futrin 2. The method recites in step (b) that a compound is assayed for binding to Futrin 2 to form a complex thereof. The method recites in step (c) "assaying the Futrin 2/binding partner complex to determine if the binding partner affects the activity of the Futrin 2 polypeptide". This would be clearer if recited as --(c) assaying the Futrin 2/binding partner complex to determine if the activity of the Futrin 2 polypeptide is altered--. The method does not really determine if the binding partner affects the activity only if binding affects the activity. As

well, the recitation in the preamble that the compound affects "the activity" implies there is only one activity. If this is the case, it would be clearer to indicate what this activity is. If not then the claim should be amended to recite --an activity-- in the preamble.

Claim 30 recites that "the binding partner is further tested as a drug candidate for disorders associated with Wnt signaling". For consistency as well as accuracy, the claim should recite, --candidate for a disorder-- as claim 31 recite, the disorder is.

Appropriate correction is required.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 26 and 30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 26 and 30 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: in claim 26, the missing step is when the level of expression is measured. Typically, expression occurs in a cell or in an *in vitro* assay buffer. However, there is not indication of the Futrin 2 being in a cell or expression system. Hence, it is not clear when expression occurs such that it can be measured. In claim 30, the missing step is how the "binding partner" is tested as a drug candidate for a disorder associated with Wnt signaling.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of identifying a binding partner for futrin 2 (SEQ ID NO:26) wherein the method comprises contacting SEQ ID NO:26 with a compound to be screened wherein binding is assayed and compounds that bind are identified as binding partners, does not reasonably provide enablement for any other embodiment. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. **This rejection is maintained for reasons of record in the office action mailed**

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the patent coupled with information known in the art without undue experimentation (*United States v. Telectronics, Inc.*, 8 USPQ2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is required is not based on a single factor but is rather a conclusion reached by weighing many factors (See *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter, 1986) and In *re Wands*, 8USPQ2d 1400 (Fed. Cir. 1988); these factors include the following:

The MPEP teaches, "However, claims reading on significant numbers of inoperative embodiments would render claims non-enabled when the specification does not clearly identify

the operative embodiments and undue experimentation is involved in determining those that are operative. Atlas Powder Co. v. E.I. duPont de Nemours & Co., 750 F.2d 1569, 1577, 224 USPQ 409, 414 (Fed. Cir. 1984); In re Cook, 439 F.2d 730, 735, 169 USPQ 298, 302 (CCPA 1971). (see MPEP 2164.08(b). First, the instant claims are drawn to a method of identifying a binding partner of futrin 2 which is identified as SEQ ID NO:26. The method comprises contacting futrin 2 with a compound and "determining whether the compound affects an activity of the polypeptide or whether binding of the compound to futrin has occurred". The method is designed to identify binding partners and to this end it is not clear how the step of "determining whether the compound affects an activity of futrin" is capable of achieving such a goal as such as compound need not bind to affect activity. The only indication of a compound that is a binding partner is one in which binding activity is detected and hence this step is required of the methods.

Secondly, Applicants have added new claims 25, 26 and 29 drawn to methods of determining the amount of compound bound to futrin 2 as a measure of levels of futrin 2 55as well the level of expression is compared to a control and thus provides an indication of a disease associated with aberrant expression of futrin 2. While the claims have been newly added, support is not found in the specification for such steps and hence is not found in the priority documents. Therefore, these claims constitute NEW MATTER. As set forth above, it is not clear how determining the amount of compound bound to futrin 2 provides a measure of level of expression of the futrin 2. The method of determining binding of a test compound to a peptide is typically done *in vitro* and hence levels of peptide added are at the discretion of the practitioner. Hence, it appears as if claims 25 and 26 are limited to a cellular measure of binding. These steps are not clearly set forth. However, even given a cellular binding state, it is not clear how binding

of a compound correlates to a *level of expression* of a protein i.e. a step of production of the protein and the specification is absent any steps that would provide such ability to correlate.

Even should a measure of binding be correlative with levels of futrin 2 in a cell, absent a clear control, it is not clear how the levels can be used as an indicator of disease. The physiological art is recognized as unpredictable. (MPEP 2164.03.) In cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws. In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved. Applicants propose a number of diseases and disorders that are associated with aberrant futrin 2 expression, however, it is not clear that these are art accepted claims and hence, the ability to identify a disease that is associated with futrin 2 aberrant expression is unclear. Secondly, the control level is critical in this type of experiment. However, no such control has been identified and furthermore, the claim does not set forth a clear connection between the expression level and the relationship with a disease.

Thirdly, the recitation in claims 23 and 28 that the "compound inhibits the activity of the futrin 2 polypeptide" or :the compound exhibits agonist or antagonist activity" are "reach-through" claims that requires possession of a compound identified through the claimed methods. The written description requirement under 35 USC 112, first paragraph may be met by sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical

and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between structure and function, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. Applicant is referred to the Guidelines on Written Description published at FR 66(4) 1099-1111 (January 5, 2001) (also available at www.uspto.gov). In this case, the compound is an unidentified compound whose activity is to be tested in the method claims that are recited. Hence, one cannot know what the activity of the compound is prior to the assay.

Claim Rejections - 35 USC § 102 or 103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 21-24, 27, 28, 30 and 31 are rejected under as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Tang et al WO 01/77169. **This is a new rejection.**

The instant application teaches that Futrin 2 was previously identified

> [0012] During the experiments resulting in the present invention four genes, futrin 1, 2, 3 and 4, could be identified the products of which are modulators of the Wnt pathway. Futrin 2 was previously identified as hPWTSR (Chen et al., 29 (2002), Mol. Biol. Rep. 287-292), a protein of before unknown role or function, expressed in numerous cell types. Further, human Futrin 1, 2, 3, and 4 were described as Stem Cell Growth Factor-Like Polypeptides, which are able to promote proliferation of hematopoietic stem cells (WO-A-01/77169; WO-A-01/07611).

Tang et al teaches use of the peptides in methods of determining binding partners (see e.g. page 88, lines 8-20). This peptide would inherently have the sequence of SEQ ID NO:26. The test compound can be an antibody (see e.g. page 133, line 5-10, page 134, line 11-23,. Section 5.17). Such immunological assays and binding assays cited traditionally include means to determine amount of antibody or compound bound (see e.g. page 151, line 10-29, i.e. radio-immunoassays). As well as binding, affect of activity of the peptide is analyzed (see e.g. page 109, line 5-22, 12-18, section 5.9.14 and 5.18) as well as level of expression (see e.g. section 5.18). The compound can be tagged (see e.g. page 109, line 19-24, page 134, line 11). It is noted that binding assays typically are drawn to addition of a known amount of peptide with a test compound followed by a measure of amount of bound and unbound peptide. Hence, a practitioner would following classic methods of binding assays determine the level of protein before and after binding. The compounds are used for treatment such as cancer (see e.g. 5.9.16).

Claims 10, 21-24, 27 and 28 are rejected under as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Warren et al WO 02/060492 published 8/2/2002, rejection based upon 20040077048. **This is a new rejection based upon amendment to reject the claims under obviousness as opposed to anticipation.**

Warren et al teach a peptide highly similar to SEQ ID NO:26 wherein the method comprises detecting binding of the polypeptide to a test compound (see e.g. SEQ ID NO:12 and ¶ 0045). The test compound can be an antibody (see e.g. ¶ 0201). As well as binding, affect of activity of the peptide is analyzed (see e.g. ¶ 0202). The compound can be tagged (see e.g. ¶

0203). It is noted that binding assays typically are drawn to addition of a known amount of peptide with a test compound followed by a measure of amount of bound and unbound peptide. Hence, a practitioner would following classic methods of binding assays determine the level of protein before and after binding. As well, these compounds are used to test as treatment (see e.g. 0043 and 0021).

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Qy          1 MQFRLFSFALIILNCMDYSHCQGNRWRRSKRASYVSNPICKGCLSCSKDNGCSRCQQKLF 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MQFRLFSFALIILNCMDYSHCQGNRWRRSKRASYVSNPICKGCLSCSKDNGCSRCQQKLF 60

Qy         61 FFLRREGMRQYGECLHSCPSGYYGHRAPDMNRCARCRIENCDSCFSKDFCTKCKVGFYLH 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 FFLRREGMRQYGECLHSCPSGYYGHRAPDMNRCARCRIENCDSCFSKDFCTKCKVGFYLH 120

Qy        121 RGRSFDECPDGFAPLEETMECVEGCEVGHWSEWGTCSRNNRTCGFKWGLETRTRQIVKKP 180
              ||| ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 RGRCFDECPDGFAPLEETMECVEGCEVGHWSEWGTCSRNNRTCGFKWGLETRTRQIVKKP 180

Qy        181 VKDTIPCPTIAESRRCKMTMRHCPGGKRTPKAKEKRNKKKKRKLIERAQEGHSVFLATDR 240
              |||||||||||||||||||||||||||||||||||||||||||||||| |||||||||
Db        181 VKDTIPCPTIAESRRCKMTMRHCPGGKRTPKAKEKRNKKKKRKLIERAQEQHSVFLATDR 240

Qy         241 ANQ 243
               |||
Db         241 ANQ 243
```

Response to amendment

The peptide of Wang et al is a newly identified and loosely characterized protein whose sequences are related by 99.1% to SEQ ID NO:26. The argument that it is not Futrin 2 seems a bit premature given that no such comparison has been made. Considering the chances that this sequence is a variant of Futrin 2, one must consider the sequences that are mutated. It is clear that two such mutations would not render a completely new protein. However, absent these mutations, the protein is 100% identical to Futrin 2. Such a protein would be expected to have Futrin 2 activity. Therefore, the issue is, does the presence of the two substitutions alter the

Futrin 2 activity. In other words, should these mutations be introduced into Futrin 2, would that protein's activity be altered. Given the lack of structural information in the specification as well as the art and absent evidence to the contrary, the molecules would be expected to encode similar proteins with similar binding capabilities.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MARIA B. MARVICH whose telephone number is (571)272-0774. The examiner can normally be reached on M-F (7:00-4:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, PhD can be reached on (571)-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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